REMARKS

These remarks are in response to the Office Action dated August 9, 2006. Applicants have canceled all previously pending claims. New claims 61-81 have been added to clarify the claimed inventions. Support for the new claims can be found throughout the specification as filed. For example, support for the recitation of "matrix" in new claim 61 can be found at page 5, lines 24-26, bridging to page 6, lines 1-4 of the specification as filed. Support for the recitation of "controlled release" and "once daily administration" in new claim 61 can be found at page 4, lines 20-24, bridging to page 5, lines 1-4 of the specification as filed. Support for the recitation of a hydrophilic component that forms a "viscous layer in an aqueous medium through which the clarithromycin or clarithromycin derivative diffuses upon solubilization" in new claim 65 can be found at page 5, lines 1-4. Support for the recitation of "a mixture of HPMC and HPC" in new claim 79 can at page 6, last paragraph, bridging to page 7, first paragraph of the specification as filed. Support for the recitation of combining the components of the pharmaceutical formulation "to allow the fatty component to form the matrix" and dispersing the "hydrophilic component and the clarithromycin component" within the matrix in new claim 80 can be found at page 4, lines 20-24, bridging to page 5, lines 1-4 of the specification as filed. Additional support can be found at page 6, lines 12-18, of the specification as filed.

No new matter is believed to have been introduced. Claims 61-81 are pending and at issue. Applicants request reconsideration of the pending claims.

INFORMAL MATTERS

Applicants wish to thank Examiner Gollamudi for the helpful discussion with Applicants representatives on Thursday, January 11th.

I. REJECTION UNDER 35 U.S.C. §112, SECOND PARAGRAPH

Claims 20-21, 30, 34, and 38-39 stand rejected under 35 U.S.C. §112, second paragraph, as allegedly being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. This rejection is moot with regard to canceled claims 20-21, 30, 34, and 38-39. While Applicants traverse this rejection, it is believed that new claims 61-81 clearly and distinctly identify the subject matter of the claimed pharmaceutical compositions.

Accordingly, Applicants request that the rejections under 35 U.S.C. § 112, second paragraph be withdrawn.

II. REJECTION UNDER 35 U.S.C. §102(b)

Claims 45 and 50-52 stand rejected under 35 U.S.C. §102(b) as allegedly being anticipated by Briskin et al. (WO 95/22319). This rejection is moot with regard to canceled claims 45 and 50-52. While Applicants traverse this rejection, it is believed that new claims 61-81 are not anticipated by the cited reference. Accordingly, Applicants request that the rejection under 35 U.S.C. § 102(b) be withdrawn.

III. REJECTION UNDER 35 U.S.C. §103

Claims 16, 17, 22, 24-30, 34-36, 40, 42-44, 46, 48, 53-54, 56, and 58-60 stand rejected under 35 U.S.C. 103(a) as being unpatentable over Briskin et al. (WO 95/22319) in view of Gibson et al. (U.S. Patent No. 5,811,120). This rejection is moot with regard to canceled claims 16, 17, 22, 24-30, 34-36, 40, 42-44, 46, 48, 53-54, 56, and 58-60. Applicants traverse this rejection and will now address any issues that may be raised by the pending rejections with regard to new claims 61-81.

Applicants respectfully aver that any rejection of the new claims based on the combination of the cited references, in view of the instant disclosure, would constitute improper hindsight. Applicants submit that no specific understanding or principle within the knowledge of the skilled artisan would motivate one to combine the cited references in the absence of any knowledge of the instant disclosure. Even if the references were so combined, the skilled artisan would have no expectation of success in generating the claimed inventions in the absence of such knowledge.

The present claims are drawn to pharmaceutical formulations, and methods of producing such formulations, that include a fatty component, a hydrophilic component, and a clarithromycin component. Applicants were the first to discover that these components could be combined to form a matrix that sustains the release of clarithromycin over a 24 hour period of time with a high degree of reproducibility (see e.g., instant specification as filed, bottom of page 4, bridging to page 5). The instant specification teaches a matrix that releases clarithromycin through the combined modalities of fatty component disintegration and hydrophilic component

formation of viscous microenvironments (see e.g., instant specification as filed, bottom of page 5, bridging to page 6).

Briskin et al. describes a formulation that includes the components clarithromycin, povidone K90, carbopol, hydroxypropyl cellulose, glyceryl behenate, and microcrystalline cellulose (see Table 1, part 1b). It is clear from the specification of the cited reference that Briskin fails to appreciate the significance of forming a matrix with these components, or any combination thereof, in order to facilitate the controlled release of clarithromycin over an extended period of time. For example, and in contrast to the claimed invention, the hydrophilic component "carbopol," as included in the Briskin formulation was not used as a release-controlling agent in a matrix. Instead, carbopol was used as a suspending agent or stabilizer in the pharmaceutical preparations described by Briskin. While the cited reference recites various hydrophilic polymers that can be included in a pharmaceutical formulation, Briskin clearly fails to disclose any matrix that utilizes a hydrophilic component to facilitate, in conjunction with a fatty component, the controlled release of clarithromycin over a period of 24 hours. Instead, Briskin describes the use of "coatings" to control the disintegration of the formulation in a aqueous environment. Clearly this reference supplies neither motivation to use hydrophilic polymers in conjunction with fatty components to arrive at a controlled-release pharmaceutical formulation containing a matrix as set forth in the new claims, nor any expectation of success if one were to attempt it.

Gibson et al. and Evenstad et al., have been cited for their teachings regarding conventional hydrophilic binders and high viscosity hydrophilic binders. Applicants acknowledge that each of these secondary references provides general information about hydrophilic binders. However, neither reference remedies the deficiencies of Briskin because neither Gibson nor Evenstad suggests a matrix formulation utilizing a hydrophilic polymer in conjunction with a fatty component to arrive at a formulation for the controlled-release of clarithromycin. There is simply no motivation in either Gibson or Evenstad to experiment with hydrophilic polymers and fatty components to generate a matrix suitable for use in a formulation for the once daily administration of clarithromycin, and certainly no teaching that such experiments would have any likelihood of success.

The inventions claimed in new claims 61-81 would not be obvious in view of Briskin, Gibson and Evenstad because the references alone or in combination fail to supply the requisite motivation or the requisite expectation of success in generating a pharmaceutical formulation of the invention. Any attempt to combine the disparate teachings of Briskin et al. on the one hand, and Gibson et al. and Evenstad et al., on the other, would necessarily involve hindsight gleaned only from reading Applicant's own disclosure about the newly discovered matrix formulation. As the Examiner is well aware, such a hindsight reconstruction is not permitted under U.S. law. The motivation to combine must come from the references themselves, and not from the Applicant's disclosure.

CONCLUSION

In summary, for the reasons set forth herein, Applicants maintain that claims 61-81 clearly and patentably define the invention. Applicants request that the Examiner reconsider and withdraw the various grounds for rejection set forth in the Office Action.

If the Examiner would like to discuss any of the issues raised in the Office Action, Applicants' representative can be reached at (858) 509-7318. A petition for a three-month extension of time, and appropriate fees, accompany the present Response. Should any additional fees be required, the Commissioner is authorized to charge deficiencies or credit any overpayment to Deposit Account No. 02-4800.

Respectfully submitted,

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